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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/974,719	10/09/2001	Dusan Ninkov	P06882US01	7844

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EXAMINER	
JAGOE, DONNA A	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/974,719	NINKOV, DUSAN	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-20 and 37-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 25 August 2004 has been entered.

Claims 4-20 and 37-43 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13, 20, 42 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 13 and 42, the phrase "of the pharmaceutically acceptable carrier of sodium chloride" in the last line of the claims renders the claim indefinite because it is unclear whether the sodium chloride is the carrier or the carrier is designed to carry the sodium chloride. Amending the claims to recite the following would obviate the rejection.

(Claim 13) " The pharmaceutical composition of claim 12 comprising an antimicrobial compound in an amount of from 0.5% by weight to 0.8% by weight and wherein the pharmaceutically acceptable carrier is sodium chloride in an amount of from 0.5% by weight to 1.0% by weight of the pharmaceutical composition".

And

(Claim 42) "The pharmaceutical composition of claim 7 comprising an antimicrobial compound in an amount of from 0.5% by weight to 0.8% by weight and wherein the pharmaceutically acceptable carrier is sodium chloride in an amount of from 0.5% by weight to 1.0% by weight of the pharmaceutical composition".

Claims 20 and 43 recites the limitation "the infection" in line 2 of the claims. There is insufficient antecedent basis for this limitation in the claim because it depends from 15 and 12 respectively and there is no "infection" recited in the claims from which these claims depend.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 4-6, 8-20 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ropapharm B.V., EP 0904780A1 (Ropapharm) in view of Avery's Drug Treatment, 4th Edition, Chapter 31, pp. 1455-1509 (Avery).

Ropapharm teaches a pharmaceutical composition in the form of a solution comprising Carvacrol and/or Thymol, water, Emulgator 686 and polysorbate as being suitable for the treatment of diseases caused by *Salmonella* spp., *Pasteurella* spp., *E. coli*, *Vibrio coli*, etc. (page 2, col. 1 line 55 to col. 2, Line 5). Furthermore, the primary reference teaches the active ingredient in the form of thymol and/or carvacrol is present in an amount of 1-10% by weight, based on the total weight of the formulation. However, the reference lacks the specific concentrations as claimed instantly in claims 14-18. Avery teaches that the dosage regimens recommended by the manufacturers of Antimicrobial drugs are purely arbitrary. The secondary reference gives guides for determining dosage amounts, but says that values will depend on the health, age, and pharmacokinetic characteristics of the patient. (Page 1489, col. 1, 4). Dosages of Antimicrobial Drugs - col. 2, 4.1 Dosages at Extremes of Age. Moreover, while the references are silent regarding the specific percentages by weight of thymol and carvacrol as claimed instantly, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is

evidence indicating such concentration is critical. As anyone of ordinary skill in the art will appreciate, changes in result effective variables are not patentable where the difference involved is one of degree, not of kind; experimentation to find *workable* conditions generally involves no more than the application of routine skill in the art of chemical engineering. See, only as exemplary, the dicta of *In re Aller* 105 USPQ 233. Similarly, the determination of *optimal* values within a disclosed range is generally considered obvious. See, only as exemplary, the dicta of *In re Boesch* 205 USPQ 215.

For these and other self-evident reasons, it would have been obvious to one having ordinary skill in the art at the time the inventions was made to have modified the composition of Ropapharm comprising thymol and carvacrol by adjusting the concentrations of the antimicrobial drugs as suggested by Avery because of the reasonable expectation of obtaining a composition comprising a mixture of thymol and carvacrol which would be capable of treating diseases caused by bacterial infections.

Claims 4-9, 12-20 and 37-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ropapharm B.V. EP 0904780A1 and further in view of Remington's Pharmaceutical Sciences, 15th Edition, 1975, pages 1405-1412.

Determining the scope and contents of the prior art

Ropapharm teaches a pharmaceutical composition in the form of a solution comprising Carvacrol (isopropyl o-cresol) and or Thymol (applicants refer to Thymol as isopropyl-cresol), water, Emulgator 686 and polysorbate (page 3, column 1, line 50 to column 2, line 17). The reference teaches the pharmaceutical compositions as being suitable for the treatment of diseases caused by *Salmonella* spp., *Pasteurella* spp., *E.*

coli, *Vibrio coli*, etc. (page 2, column 1, line 55 to column 2, line 5). The reference teaches the active ingredient in the form of thymol and/or carvacrol is present in an amount of from 1 to 10% by weight based on the total weight of the formulation (page 2, column 2, lines 49-56) for treatment of poultry, including turkeys, as in instant claim 19 and the use as an injectable composition comprising both thymol and carvacrol in amounts which overlap those claimed in instant claims 8-9 and 12, for the treatment of diseases caused by infections of instant claim 20.

Ascertaining the differences between the prior art and the claims at issue

The primary reference lacks the sodium chloride of instant claim 13 and 42. Remington teaches that knowledge of colligative properties of solutions is essential for one to understand fully the principles involved in rendering intravenous solutions isotonic with blood serum. To produce less shock and less irritation than those which are hypotonic or hypertonic, and present-day practice recognizes the desirability of making the necessary adjustment whenever possible. Finally, the secondary reference teaches that the usual practice is to add wither sodium chloride or dextrose to adjust hypotonic intravenous solutions to isotonicity (page 1405, column 1, line 1 to page 1406, column 1, line 34).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the isotonicity of the injectable formulation of Ropapharm by adjusting the tonicity of the solution using sodium chloride, the salt which is usually used for adjusting tonicity of injectable solutions because of the reasonable

expectation that sodium chloride would adjust the formulation to produce less shock and less irritation.

Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ropapharm B.V., EP 0904780A1 (Ropapharm) and further in view of Remington's Pharmaceutical Sciences, Fifteenth Edition, 1975, pp.1405-1412 as applied to claims 4-9, 12-20 and 37-43 above, taken together with The Merck Index, An Encyclopedia of Chemicals, Drugs, and Biologicals 12th Edition, 1996 page 9539 (Merck) and common knowledge in the art.

The combined references above teach a solution comprising Carvacrol (isopropyl o-cresol) and/or Thymol (isopropyl-cresol), water, Emulgator 686 and polysorbate, which is adjusted for isotonicity using either sodium chloride or dextrose, however, the combined references lack the specific oils of claims 10-11.

The Merck Index, An Encyclopedia of Chemicals, Drugs, and Biologicals, 12th Edition, 1996, page 9539 (Merck).

Merck teaches 1 gram of Thymol dissolves in 1.7 ml olive oil at 25 degrees. Since this is a claim to a composition, and the intended use of said composition is not given patentable weight unless it results in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. Since Merck teaches the specifically claimed antimicrobial compound in the specifically claimed pharmaceutically acceptable carrier, it meets the limitations of instant claims 11. It is common knowledge that vegetable oil is a cheap, easily obtained alternative to olive oil.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the solution comprising Carvacrol (isopropyl o-cresol) and/or Thymol (isopropyl-cresol), water, Emulgator 686 and polysorbate, which is adjusted for isotonicity using either sodium chloride or dextrose, by adding olive oil as suggested by Merck, or by using a cheaper, easily obtained vegetable oil, because of the reasonable expectation of obtaining an injectable pharmaceutical composition, comprising a readily available pharmaceutically acceptable carrier, which has the desirable property of solubilizing thymol.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday and Thursday from 9:00 A.M. - 7:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Donna Jagoe
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12/10/2004

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